Induced Pluripotent Stem Cells for Tissue Regeneration

Grant Award Details

Induced Pluripotent Stem Cells for Tissue Regeneration

Grant Type:	Basic Biology III
Grant Number:	RB3-05232
Project Objective:	The project is using peripheral nerve regeneration as a model to test the matrix and scaffolding needs to facilitate iPSC-derived NCSC transplantation.

Investigator:

Name:	Song Li
Institution:	University of California, Berkeley
Type:	PI

Disease Focus:	Neurological Disorders, Neuropathy
Human Stem Cell Use:	iPS Cell
Award Value:	$1,209,148
Status:	Closed

Progress Reports

Reporting Period:	Year 1
View Report	

Reporting Period:	Year 2
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Reporting Period:	Year 3
View Report	

Grant Application Details

Application Title: Induced Pluripotent Stem Cells for Tissue Regeneration

Public Abstract: Induced pluripotent stem cells (iPSCs) have tremendous potential for patient-specific cell therapies, which bypasses immune rejection issues and ethical concerns for embryonic stem cells (ESCs). However, to fully harness the therapeutic potential of iPSCs, many fundamental issues of cell transplantation remain to be addressed, e.g., how iPSC-derived cells participate in tissue regeneration, which type of cells should be derived for specific therapy, and what kind of matrix is more effective for cell therapies. The goal of this project is to use iPSC-derived neural crest stem cells (NCSCs) and nerve regeneration as a model to address these fundamental issues of stem cell therapies. NCSCs are multipotent and can differentiate into cell types in all three germ layers (including neural, vascular, osteogenic and chondrogenic cells), which makes NCSC a valuable model to study stem cell differentiation and tissue regeneration. Peripheral nerve injuries and demyelinating diseases (e.g., multiple sclerosis, familial dysautonomia) affect millions of people. Stem cell therapy is a promising approach to cure these diseases, which will have broad impact on healthcare.

This project will advance our understanding of how extracellular microenvironment (native or engineered) regulates stem cell fate and behavior during tissue regeneration, and whether stem cells such as iPSC-NCSCs and differentiated cells such as iPSC-Schwann cells have different therapeutic effects. The results from this project will provide insights that will facilitate the translation of stem cell technologies into therapies for nerve injuries, demyelinating diseases and many other disorders that may be treated with iPSC-NCSCs.

Statement of Benefit to California: Induced pluripotent stem cells (iPSCs), especially iPSCs without the integration of reprogramming factors into the genome, are valuable to model disease and to generate autologous cells for therapies. Understanding the role and differentiation of iPSC-derived cells in tissue regeneration will facilitate the translation of stem cell technologies into clinical applications.

iPSC-derived neural crest stem cells (NCSCs) can differentiate into a variety of cell types, and hold promise for the therapies of diseases such as nerve injuries, demyelinating diseases, spina bifida, vascular diseases, osteoporosis and arthritis. The isolation and characterization of iPSC-NCSCs will provide a basis for their broad applications in tissue regeneration and disease modeling.

This project will use peripheral nerve regeneration as a model to address the fundamental issues of using iPSC-NCSCs for therapies. Peripheral nerve injuries (over 800,000 cases in the United States every year) are very common following traumatic injuries and major surgeries (e.g., removing tumor), which often require surgical repair. Stem cell therapies can accelerate nerve regeneration and avoid the degeneration of muscle and other tissues lack of innervation. Since iPSC-NCSCs can promote the myelination of axons, the therapies for nerve injuries could also be adopted to treat demyelinating diseases.

In many cases of stem cell therapies, matrix and scaffold materials are needed to enhance cell survival and achieve local delivery. The studies on appropriate matrix for stem cell delivery will provide a rational basis for designing and optimizing materials for stem cell therapies.

The fundamental issues addressed in this project, such as the differentiation and signaling of transplanted cells, the therapeutic effects of cells at the different stages of differentiation and the roles of delivery matrix/materials, will have implications for stem cell therapies in many other tissues.

Overall, the results from this project will advance our knowledge on stem cell differentiation and function during tissue regeneration, help us translate the knowledge into clinical applications, and benefit the health care in California and our society.